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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,462	05/22/2002	Richard D Thomas	2521-101	4462

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EXAMINER	
RINES, ROBERT D	

ART UNIT	PAPER NUMBER
3626	

NOTIFICATION DATE	DELIVERY MODE
07/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/009,462	THOMAS ET AL.	
	Examiner	Art Unit	
	Robert D. Rines	3626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Notice to Applicant

[1] This communication is in response to the patent application filed 22 May 2002. It is noted that this application benefits from Provisional Patent Application Serial No. 60/141,006 filed 29 June 1999. Claims 1-5 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[2] Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fink et al. (United States Patent #5,808,918) in view of Gray (United States Patent #5,437,279).

As per claim 1, Fink et al. disclose a computer-implemented system for simulating the occurrence and progression of disease in the human body, comprising: reference sources containing information relating to genetics, molecular biology, and population statistics as applied to occurrences and progression of human disease (Fink et al; Abstract, col. 3, lines 7-31, col. 7, lines 20-33, and Fig. 6); an operator interface for inputting into said system information and instructions corresponding to patient data (Fink et al.; col. 11, lines 35-64 and col. 13, lines 26-42); a plurality of program modules (Fink et al; col. 4, lines 36-61 and Fig. 1), each including at least one subroutine, for processing information and data inputted through said operator interface in conjunction with information obtained from reference sources (Fink et al.; col. 2, lines 63-67, col. 4, lines 37-67, col. 5, lines 1-20, col. 7, lines 17-33, and Fig. 6); and outputting said information to said operator interface (Fink et al.; col. 6, lines 13-17, col. 11, lines 35-53, and col. 13, lines 26-42), wherein each of said program modules carries out descriptive and mathematical processes corresponding to different levels of human disease processes (Fink et al.; col. 2, lines 63-67, col. 4, lines 37-67, and col. 5, lines 1-20), and information generated by modules performing lower level processes also is outputted to modules performing higher level processes (Fink et al.; col. 3, lines 24-32, col. 4, lines 13-24, and col. 4, lines 49-57), whereby predictive disease progression are provided (Fink et al; col. 3, lines 20-23 and col. 4, lines 25-35); and an output device for communicating results of subroutine processing to a user (Fink et al.; col. 6, lines 13-17 and col. 13, lines 36-42).

While Fink et al disclose the development and application of Reference Biological Patterns and Knowledge Bases as derived from a variety of information sources, in order to simulate

interrelated-biological findings and hypotheses at the cellular and subcellular levels, Fink et al. fails to specifically indicate the specific cellular, subcellular, and systems level information directed to applications of the modeling program to origin and metastases of human cancer.

However, as evidenced by Gray, such data/indicators are well known in the determination of cancer/tumor origin (i.e., determination of primary tumor) and are well known predictors of cancer metastases (Gray; Abstract, col. 2, lines 12-38 and col. 12, lines 32-42). Accordingly, such data would likely be included in the reference sources utilized by the Fink et al. invention.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Fink et al. with those of Gray. Such combination would have resulted in a functional computer model that integrates all of the biologic relationships that are known to exist and that are relevant to the particular disease of interest such that the course of a particular disease progression and impact of a particular treatment on the progression are demonstrable by the system (Fink et al.; col. 3, lines 15-24). Included in such existing known inputs would have been well known indicators/predictors of cancer origin and metastases (Gray; Abstract, col. 2, lines 12-38 and col. 12, lines 32-42). The motivation to combine the teachings would have been to predict the locations of the lymph nodes most at risk of metastasis based on the primary tumor associated with a cancer of the neck or head (Gray; col. 2, lines 12-18).

As per claim 2, Fink et al. disclose a system, which allows diagnostic, treatment and research human disease simulations to be performed by accepting user inputted information, and an

educational configuration using pre-programmed situations which allows interaction for medical student educational purposes (Fink et al.; col. 4, lines 13-35).

As per claim 3, Fink et al. disclose a customizable system wherein a plurality of program modules (see Fink: Knowledge Diagrams) simulate interrelated biological process of disease progression at the subcellular, cellular, human/anatomical, disease manifestation, clinical signs and symptoms, and clinical outcomes level (Fink et al.; col. 5, lines 8-38). Examiner considers the Fundamental Model Units provided by Fink et al., as functional equivalents of the tumor origin, cellular, colony, tissue, tumor and metastatic modules claimed by Applicant.

As per claim 5, Fink et al. disclose a computer-implemented method of simulating the occurrence and progression of disease in the human body, comprising the steps of: collecting and providing information relating to genetics, molecular biology, and population statistic as applied to occurrences and progression of human disease (Fink et al.; Abstract, col. 3, lines 7-31, col. 7, lines 20-33, and Fig. 6); providing information and instructions corresponding to patient data (Fink et al.; col. 11, lines 35-64 and col. 13, lines 26-42); processing information and data related to a patient in conjunction with said information relating to occurrences and progression of human disease and outputting said processed information (Fink et al.; col. 2, lines 63-67, col. 4, lines 37-67, col. 5, lines 1-20, col. 7, lines 17-33, and Fig. 6), wherein said processing comprises the steps of carrying out descriptive and mathematical processes corresponding to different levels of human cancer biological processes (Fink et al.; col. 2, lines 63-67, col. 4, lines 37-67, col. 5, lines 1-20) with information generated by performing lower level processes being outputted to

higher level processes (Fink et al.; col. 3, lines 24-32, col. 4, lines 13-24, and col. 4, lines 49-57), whereby predictive disease progressions are provided (Fink et al.; col. 3, lines 20-33 and col. 4, lines 25-35); and communicating the results of processing to a user (Fink et al.; col.6, lines 13-17 and col. 13, lines 36-42).

While Fink et al disclose the development and application of Reference Biological Patterns and Knowledge Bases as derived from a variety of information sources, in order to simulate interrelated-biological findings and hypotheses at the cellular and subcellular levels, Fink et al. fails to specifically indicate the specific cellular, subcellular, and systems level information directed to applications of the modeling program to origin and metastases of human cancer.

However, as evidenced by Gray, such data/indicators are well known in the determination of cancer/tumor origin (i.e., determination of primary tumor) and are well known predictors of cancer metastases (Gray; Abstract, col. 2, lines 12-38 and col. 12, lines 32-42). Accordingly, such data would likely be included in the reference sources utilized by the Fink et al. invention.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Fink et al. with those of Gray. Such combination would have resulted in a functional computer model that integrates all of the biologic relationships that are known to exist and that are relevant to the particular disease of interest such that the course of a particular disease progression and impact of a particular treatment on the progression are demonstrable by the system (Fink et al.; col. 3, lines 15-24). Included in such existing known

inputs would have been well known indicators/predictors of cancer origin and metastases (Gray; Abstract, col. 2, lines 12-38 and col. 12, lines 32-42). The motivation to combine the teachings would have been to predict the locations of the lymph nodes most at risk of metastasis based on the primary tumor associated with a cancer of the neck or head (Gray; col. 2, lines 12-18).

[3] Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fink et al. in view of Gray as applied to claim 1 above, and further in view of Lincoln et al. (United States Patent #6,303,297).

As per claim 4, Fink et al. disclose a system further comprising within each module subroutines (see Fink: Fundamental Model Units) that have responsibility over smaller descriptive and mathematical processes needed to simulate human disease progression (Fink et al.; col. 4, lines 48-57, col. 5, lines 13-28, col. 6, lines 1-4) each of the subroutines producing results in forms needed by the user to describe the biological process over which the subroutine has responsibility (Fink et al.; col. 5, lines 51-67).

The levels/strata defined by Fink et al. include Fundamental Model Units (i.e., modules) governing cell pools including controllers and regulators (i.e., cell cycle control and physical properties) (Fink et al.; col. 4, lines 62-67), a cell class group (i.e., interaction between cells routine) (Fink et al.; col. 5, lines 3-7), system function or system/body response/function (i.e., interaction between cells and a tissue structure routine) (Fink et al.; col. 5, lines 13-20) and critical clinical outcomes (i.e., a clinical outcome routine) (Fink et al.; col. 5, lines 25-28).

While Fink et al. indicates an awareness of the role of genetic mutations in disease occurrence and progression (Fink et al.; col. 6, lines 60-64), Fink et al.; fails to specifically teach the incorporation of a genetic mutation routine or analysis into the model for determination of cancer origin or metastases.

However, as evidenced by Lincoln et al., referencing a known genetic variation/mutation database in determining origin of certain cancers (i.e., a genetic mutation subroutine) is well known in the art (Lincoln et al.; col. 26, lines 24-65).

It would have been obvious to one or ordinary skill in the art at the time the invention was made to have combined the teachings of Fink et al. and Gray, as applied to claim 1 above, with those of Lincoln et al. Such combination would have resulted in a functional computer model that integrates all of the biologic relationships that are known to exist and that are relevant to the particular disease of interest such that the course of a particular disease progression and impact of a particular treatment on the progression are demonstrable by the system (Fink et al.; col. 3, lines 15-24). Further, such a combined system would have utilized existing databases that provide known relationship information between specific genetic mutations and cancer (Lincoln et al.; col. 26, lines 24-65). The motivation to combine the teachings would have been to utilize genetic information provide for the identification of the presence or progression of disorders, and to provide prognostic information on the aggressiveness of disease (Lincoln et al.; col. 1, lines 59-64).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Comanor et al., METHOD AND APPARATUS FOR PREDICTING THERAPEUTIC OUTCOMES, United States Patent #5,860,917

Paterson et al., METHOD OF GENERATING A DISPLAY FOR A DYNAMIC SIMULATION MODEL UTILIZING NODE AND LINK REPRESENTATIONS, United States Patent #6,051,029

Huo et al., METHOD AND SYSTEM FOR THE COMPUTERIZED ASSESSMENT OF BREAST CANCER RISK, United States Patent #6,282,305

Sidransky, METHOD FOR DETECTING CELL PROLIFERATIVE DISORDERS, United States Patent #6,291,163.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert D. Rines whose telephone number is 571-272-5585. The examiner can normally be reached on 8:30am - 5:00pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Thomas can be reached on 571-272-6776. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RDR

6/22/07

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